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PROGRAM REVIEW: THE LIFETIME EFFECTS OF SPACE RADIATION IN RHESUS MONKEYS

Thomas M. Butler, D.V.M, M.S.

Southwest Foundation for Biomedical Research
P.O. Box 28147
San Antonio, TX 78284

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NOTICES

This final report was submitted by the Southwest Foundation for Biomedical Research, P.O. Box 21847, San Antonio, TX 78284, under contract F33615-87-D-0627/0008, job order 7757-04-48, with the USAF School of Aerospace Medicine, Human Systems Division, AFSC, Brooks Air Force Base, Texas. Dr. David H. Wood (USAFSAM/RZB) was the Laboratory Project Scientist-in-Charge.

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The animals involved in this study were procured, maintained and used in accordance with the Animal Welfare Act and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources - National Research Council.

The Office of Public Affairs has reviewed this report and it is releasable to the National Technical Information Service (NTIS), where it will be available to the general public, including foreign nationals.

This report has been reviewed and is approved for publication.

David H. Wood

DAVID H. WOOD, D.V.M, Ph.D.
Project Scientist

S. L. Hartgraves

STANLEY L. HARTGRAVES, Lt Col, USAF, BSC
Supervisor

George Schwender MD

GEORGE E. SCHWENDER, Colonel, USAF, MC, CFS
Commander

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This report summarizes findings from a select panel of scientists charged with reviewing the quality and productivity of the USAFSAM 24-year in-house study of the lifetime effects of space radiation in the rhesus monkey. The panel also had the responsibility of assessing the value of the study in both military and civilian scientific applications and making recommendations for maximizing the yield of relevant data as the animals near the end of their life span. The panelists reviewed results presented by project scientists during a 2-day conference in San Antonio, TX, 9-10 March 1989. They were unanimous in their endorsement of the study as a uniquely important resource of information on the late effects of space radiation and the interaction of late effects with the normal aging processes. In asserting that the study should be continued for at least another 5 years, the panel made specific recommendations for additional work to be carried out in collaboration with scientists at other laboratories who could provide the breadth of technical expertise required to fully exploit the potential of this project. The scientific proceedings of the conference will be published as separate journal articles.

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CONTENTS

PROGRAM REVIEW: THE LIFETIME EFFECTS OF SPACE RADIATION IN RHESUS MONKEYS

INTRODUCTION

The commitment of the U.S. Government to manned lunar exploration in the 1960s was made at a time when the radiation hazards of such a venture were largely undefined. To help fill this urgent requirement, the U.S. Air Force School of Aerospace Medicine (USAFSAM), Brooks AFB, TX, with the support of the National Aeronautics and Space Administration, conducted a series of experiments to determine the acute and long-term effects of the types of radiation that could be encountered in extended manned space flights. Adolescent rhesus monkeys of similar age and of both sexes were exposed to single, total body doses of one of several types and energies of radiation, including protons, electrons, and x-rays. A select population of the original group of exposed animals and their age-matched controls was set aside for long-term observation of possible delayed effects.

The delayed effects study began with 301 irradiated and 57 sham-irradiated animals. The animals have been individually housed under the same environmental conditions since the study began. Though individually caged, the monkeys are in visual, aural, and tactile contact with other monkeys. No animals have been euthanized, except for humane reasons, and all animals that have died received a thorough post-mortem examination. The study is now in its 25th year and is the only existing source of controlled data on the lifetime effects of proton irradiation in a primate species. As a scientific document, the study would not be complete without a set of biological data covering the natural life span of every animal in the experiment. Unfortunately, the original experiments were not specifically designed as the basis of a lifetime study; therefore, both the biological observations and the statistical analyses have been hampered by insufficient numbers of subjects in some groups and missing data. Despite these limitations, observation of these animals has contributed to the development of improved radiation protection standards for military space crews. Recent publication by the USAFSAM of the 20-year cancer and mortality data along with new career dose limit recommendations for astronauts represents a milestone in the study.

In late 1988, 127 of the 358 original colony members were still alive. The Bibliography includes 66 scientific articles based on research data collected from the colony.

TASK DESCRIPTION AND APPROACH

The USAFSAM decided that, after 25 years, all aspects of the study on the lifetime effects of space radiations in the rhesus monkey (Macaca mulatta) should be reexamined to determine how the best interest of the U.S. Air Force and the U.S. manned space program might be served. It was also decided that the most acceptable approach for this effort would be to have a panel of independent experts provide this assessment. Under subcontract from the

Texas A&M Research Foundation, the Southwest Foundation for Biomedical Research (SFBR) selected a panel of scientists, who were not directly working for the U.S. Air Force, to assess the potential of the colony to provide additional relevant data on delayed radiation effects, to critically evaluate data collection and management procedures, and to identify the most promising approaches to the resolution of unanswered questions. The panel members are listed in Appendix A.

The panel members were selected by the principal investigator for their expertise in the scientific disciplines of radiation biology, radiation physics, pathology, aging, primatology, veterinary medicine, human medicine, genetics, and biostatistics. Each member is nationally recognized by his peers as an authority in his field and fully qualified to accomplish the described task.

The panel met on 9-10 March 1989 at the Southwest Foundation for Biomedical Research, San Antonio, TX. At that time, USAF scientists, including USAFSAM military and civilians as well as selected contractors, presented reports of past and current research and considerations for future work concerning the study of lifetime effects of radiation in rhesus monkeys. The presentations are listed by title in Appendix B. Draft manuscripts on these topics were prepared by the presenters and distributed to each panel member in advance of the meeting.

The panel was also charged with reviewing the manuscripts for publication in the journal, Radiation Research. Critiques of the manuscripts were provided to the authors separate from this final report.

PANEL REPORT[1]

The experiment to study the effects of proton radiation on rhesus monkeys began in 1964 under the direction of Dalrymple, Lindsay, and their colleagues.[2] The aim of the project was to provide information about possible effects of radiation in space. It was an ambitious undertaking. Protons predominate in the radiation environment in space and they have a broad energy spectrum. The experiments included exposures to 5 proton energies, from 32 MeV to 2300 MeV, in order to obtain information for a reasonably representative spectrum of energies. The experiment is unique and has provided interesting and important information. It is clear that there is considerable potential for providing equally important data in the future.

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1. A summary of the report of the panel as submitted by the chairman, Dr. R. J. M. Fry.

2. The panel was pleased to have both Dr. Dalrymple and Air Commodore Lindsay at the meeting to discuss the earlier work.

The return on the investment of time, expertise, and money in the original experiments came quickly in the case of acute effects. The results of the assays of lethality after acute high doses of radiation were published promptly. Since then, progress and interim reports on the late effects have appeared as the data accumulated. It will be some years before the final chapters on tumor induction, life shortening, and nonstochastic effects can be written; nevertheless, it is very important that it be done.

The determination of late effects, such as cancer and degenerative diseases, is a lengthy process and to obtain the full return requires unusual persistence, management skills, and support. The colony has been maintained in an exemplary manner. The median survival time of the control monkeys is 24 years. This is higher than for any other colony of rhesus monkeys in the nation and attests to the remarkable care that these animals have received. It is clear that there has been a remarkable commitment to the care of the animals and the management of the project. As a result of the success in maintaining this colony, there are now two resources. The colony, which now stands at 88 irradiated monkeys and 29 control nonirradiated animals, is a resource not only for further information about the effects of proton radiation but also for gerontological studies. How long it should be maintained cannot be answered now. It is clear that the ideal would be to follow out the experiment to the end because each of the old monkeys can produce useful information. In relatively small sample sizes one or two monkeys can make a difference, especially in the case of cancer incidence. We recommend, unequivocally, that the colony be maintained and that the case for further maintenance should be reviewed in about 5 years.

In all lifetime radiation studies, especially studies on large animals, there is the conflict between minimal intervention, so as not to compromise the objective of obtaining the data for late effects, and the desire to obtain as much data as possible at each stage of the study, which necessarily entails intervention. This study is no exception. The panel has made certain recommendations, which are described herein, but their exposure to the actual work and the staff was brief. They acknowledged that there may be practical aspects of which they were unaware and which could have influenced their suggestions; some of which will involve more intervention with the animals than is currently accepted.

The panel felt that the project could benefit from more collaborative studies and interaction with research workers in other institutions. A diversity of expertise is required to exploit the potential of this colony of rhesus monkeys to its fullest. Such collaborative studies should enhance the research produced by the team at USAFSAM in both breadth and quality. Some of the suggestions for collaborative work would entail extra examinations of the animals and perhaps more sampling than is currently permitted or planned. Decisions will have to be made about whether increased intervention in the animals will have an unacceptable impact on carrying out the initial objective or compromises the original experimental design. In general, it is our opinion that with care, there will be a benefit from obtaining more information although it does involve more intervention. The veterinarians intervene, quite correctly, in cases of disease, especially when medical and

surgical procedures are carried out. However, such procedures also impact on the studies of mortality. In order to capitalize on this resource for gerontological and radiobiological studies, more intervention should be considered. The philosophy and policies of the control of the experimental design should be reviewed for adequacy, consistency, and practicality. If the investigators have to design their experiments around semiannual examinations, there will be severe restrictions on the information that can be obtained.

The collaborative studies, on dosimetry, cataracts, and immunology that are underway, are a good example of what can be done and are to be commended. There are a number of other areas of investigation that have potential and should be explored. A number of suggestions for interaction and collaboration are mentioned below in the sections on the specific areas of research. The research team at Brooks AFB has obviously considered collaborative studies in a number of areas. The review panel suggests that such areas as neuroscience, behavioral sciences, and molecular biology could be extremely fertile areas for collaborative research and should be considered. Names of potential collaborators or researchers that might interact with the USAF team are given in Appendix C.

The potential for future investigations, by both the research staff at Brooks AFB and collaborators, will be greatly enhanced if state-of-the-art laboratory methodology is available for the collection and processing of valuable tissues. The panel recommends that the attainment, fixation, and other methods of maintenance of samples be reviewed immediately and advice sought where necessary. Storage of DNA, or tissues from which DNA can be obtained at a later date, would make it possible to use both current and future techniques in molecular biology. Immortalization of fibroblasts and lymphocytes, in order to establish specific cell lines, should be considered. Samples for the sake of samples is neither wise nor economical, but this resource is unique and every possibility of extracting information should be taken.

In its assessment of the value of the current studies, the panel summarized its impressions of each area of study as presented by the principal investigators.

Dosimetry

Overall, the dosimetry has been carried out well and carefully, and the varied circumstances have been evaluated dosimetrically; however, several additional dosimetry studies should be seriously considered. Further work should be carried out on the identification and distribution of secondary radiation which becomes an important consideration at higher proton energies. The head of the juvenile rhesus monkey could be examined in a CAT scan in order to determine whether the location of hot spots and the site of origin of the tumors coincide. Above a critical proton energy level, irradiation effects in the brain become important. Calculations based on data from CAT scans, which take into account the variation in size of the human head, should be made to determine the critical proton energy range. Drs. Wilson and

Townsend at NASA (Langley) and W. Schimmerling (Lawrence Berkeley Laboratory) are studying heavy ion irradiation of the head and interaction with them would be worthwhile.

Tissue depth dosimetry should be carried out for each of the fatal cancers. The circumstances of each monkey should be evaluated so that the organ dose for the cancer concerned is specified in detail. For uniform irradiation this should be straightforward, while for nonuniform exposure specific work will have to be done.

Biological dosimetry, while not normally in the domain of the physicists,is worth considering. These animals represent a good test (dose up to 8 Gy given 20 years ago) of the persistence of chromosome aberrations. Both fibroblasts and lymphocytes could be assayed. If the cytogenetic study, which should include the current techniques, cannot be done at Brooks AFB, one of a number of cytogeneticists could be asked to collaborate (see Appendix C).

Mortality

All of the control monkeys should be maintained for their life span, but there is the question of whether some of the irradiated monkeys, perhaps in the lower proton energy group, might be dedicated to other experimental work. It is important that the causes of death in both the control and irradiated groups be established precisely. Determination of the contribution of the different causes of death to radiation-induced excess risk is particularly important.

It should be kept in mind that the studies on the monkeys may provide an important point in the pattern of species-dependent life span and radiation-induced life shortening. The results could provide information that could be used in the modeling of extrapolation of risks across species.

Despite the small number of animals, stratification by dose, sex, energy, cause, and age should be undertaken. Obviously, there will be a number of empty cells, but the exercises should point the way for compiling the most useful data for life-table type analysis.

Interventions have been carried out for humane reasons to prolong life. Humane policies are essential, whether implemented by euthanasia or surgical or medical intervention; however, for experimental purposes, times of natural deaths from untreated diseases could be estimated and the estimates applied to the cases which were treated, in order to eliminate the influence of intervention on the data to some considerable extent.

Cataracts

The formation of cataracts is a potential late effect of radiation in deep space that is of concern. In solar particle events, relatively high doses from low-energy protons that do not penetrate to the deep organs could

be incurred, thus posing a risk of cataracts in later life. There are no data on which to base a threshold dose for cataract induction in humans by protons, nor are there data for the effects of heavy ions on the human lens. There is not unanimous acceptance of any of the experimental animal model systems that are commonly used for studies of cataract induction and certainly not for the extrapolation of the risks determined from the animal models. Thus, the studies on this primate and especially for exposures to a range of proton energies are very important. This study is being carried out as a collaborative study between outside investigators and a member of the USAF research team. The arrangement has the added advantage that the collaborators have assessed radiation cataracts in other species and are applying the same criteria and scoring system used in the other experimental animals. The same investigators have also collaborated on a number of studies of radiation-induced cataracts in other species, especially with heavy ions; therefore, species comparison and formulation of methods of extrapolation should be on a sound basis.

The mechanism of radiation-induced cataractogenesis is still a matter of dispute. It should be possible, with collaboration, to investigate the nature of the proteins in the aberrant lens fibers and the specific lesion in the DNA of the cells in the germinative zone that could have caused the change. Another important question is whether there is any evidence of regression and what influences lack of progression. Unfortunately, it may be too late to answer these questions. It is important that every possible investigation that might shed light on the loss of transparency in the lens after irradiation should be considered and carried out where possible.

Cancer

The cancer data have been carefully collected, but more thorough and complete analysis is needed. Sex-specific cancer mortality should be analyzed and the cancer mortality compared with mortality from other causes by dose group. It is noted that the recent data from the study suggest that the period of excess risk in the irradiated monkeys may be over. The question of a decrease and perhaps disappearance of excess risk with time after irradiation is very important. With the possible exception of leukemia, the data are not consistent. The reason for the lack of excess radiation-induced leukemias should be investigated. The role of retroviruses in the manifestation of late effects, especially cancer, may be a profitable area of exploration. Protocols should be set up for obtaining tissues and preserving them suitably for possible studies of changes in the genome. Chromosomal studies should be considered. Also, it would be very interesting to have some indication of the frequency of chromosome aberrations in bone marrow or circulating stem cells.

Endometriosis

Endometriosis is an important pathological condition in women. The disease in the monkeys at Brooks AFB provides an excellent model for the study

of the etiology, pathogenesis, and therapy of endometriosis. The colony, which is the largest known collection of monkeys with endometriosis, is a remarkably valuable resource and the research group at Brooks AFB has published a series of outstanding referenced articles on endometriosis. In fact, most of the information in the literature about endometriosis in monkeys has come from these studies.

The therapy of endometriosis is still a matter for investigation. These monkeys provide a singular model for both the study of etiology and the treatment of the disease. If it is possible to commit some of the monkeys to such research, the information gained could make an important contribution to the medical community. Because endometriosis is becoming an increasing problem in other monkey colonies, the USAFSAM group might consider preparing a concise but well referenced paper for the Journal of Medical Primatology. This paper would be in addition to that planned for Radiation Research. The decision of how to use the dwindling number of monkeys to best advantage will not be easy, but some well designed studies of the pathogenesis and management of endometriosis should be a carefully considered option.

Hematology and Biochemistry

There have been regular weighings of the monkeys and sampling of blood for routine hematological and biochemical analyses. It has been concluded that white blood cell counts and protein and glucose levels were altered by proton irradiation in a dose-dependent way as both an acute and a late effect. The importance of unequivocal negative findings should not be forgotten. Presumably the protocol for this study was set up many years ago with tests that were standard at that time. If serum has been stored, other tests now in common use should be utilized to maximize the data obtained. It would appear worthwhile to consult with a number of people, especially those now involved in other studies, such as endometriosis, in order to include tests that would have specific use. Of particular importance to the future work is the encouragement of the statistics group at USAFSAM to be involved in any analysis that is carried out. To make the analyses productive, certain questions should be formulated. The question should be based on the experience reported in other studies.

There are data for both the acute and late effects of irradiation for many hematological and biochemical end points in humans and also some data for monkeys. The work at TNO in The Netherlands should definitely be examined. The studies on the monkeys should be in the context of the human studies and, where possible, extensions of these studies. Obviously the experimental design restricts the spectrum of tests that can be carried out, but tests of function should be considered in the higher dose survivors and controls.

Skin Effects

This part of the study is designed to test the hypothesis that exposure to proton radiation at a relatively young age reduces the proliferative capacity of skin fibroblasts later in life. It has been noted that cells in

vitro complete a number of cell population doublings. The number of cell doublings is dependent on the age of the animal from which the cells are derived and put into in vitro culture. The potential for cell proliferation, at least as tested in vitro, decreases with age.

Normal cells have a limited capacity to proliferate; a fact that distinguishes them from transformed or "immortalized" cells. It has been disputed whether the limitation in proliferative capacity of stem cells in vivo is either detectable or important in nonirradiated humans and experimental animals. There are no adequate data about the age changes in stem cell function and certainly not about the combined effect of age and radiation injury. These studies are important and will require considerably more work before precise interpretations can be made.

Much of the work carried out on in vitro senescence has depended on the assay of cell population doublings. In order to interpret what changes have occurred with age or irradiation, it is necessary to determine whether the number of cells contributing to proliferation or the capacity to proliferate, or both, have changed. These alternatives cannot, of course, be distinguished from data on cell population doubling. It would be useful to determine if the DNA content of the cells changes as a function of age and irradiation. Flow cytometry would be helpful in the studies.

The studies of wound healing should provide a functional assessment of the ability of the cell populations involved in healing to proliferate. Expert histological examinations of the skin in the aged controls and the irradiated monkeys should be carried out. In particular, information about the state of the vasculature is important for the interpretation of any observed changes in wound healing. Pigment cell function and hair growth are other facets of the skin that might be studied by collaborators.

Induced Radiosensitivity

To investigate whether the irradiated animals retain an increased sensitivity to radiation, fibroblasts from the skin of control and proton-irradiated monkeys were cultured and their survival response to 55 MeV protons and Cobalt-60 gamma rays was determined. The results were compared with those from Chinese hamster ovary (CHO) cells, a common tissue culture model. The survival response of CHO cells appears to be the same for both gamma rays and 55 MeV protons. In contrast, both the control and previously irradiated monkey fibroblasts are slightly more sensitive to protons than to gamma rays. Analysis of the survival curves of the monkey cells shows a pattern consistent with increased radiosensitivity. When CHO cells were exposed to protons prior to the determination of survival curves for gamma radiation, the pattern was different, suggesting that the changes were due to alteration in repair rather than in the damage. There has been an increased interest in radiosensitivity of cells induced by different types of radiation and in the interactions of radiations. No such studies have been carried out with protons. If the induction of radiosensitivity in cells that were irradiated in vivo many years ago can be confirmed, it would be of considerable value in radiation risk assessment; however, the demonstration of changes in radiosensitivity must be

carried out with precision because such changes are seldom large. The results must be reproducible and the statistical analysis must be rigorous.

Immunocompetence

A collaborative study with Dr. William Stone of Trinity University, San Antonio, and Dr. Michael Miller of the University of Texas Health Science Center at San Antonio, has been underway for the past 4 years, but these observations on the immunocompetence of the aging control and irradiated monkeys have been limited by the restricted access to whole blood samples. Presumably this restriction has been considered necessary for the maintenance of the original experimental design. The current plan is to include determinations of T and B lymphocyte populations, immunoglobulin levels, cell mediated immunity, complement levels, and autoantibodies.

Drs. Stone and Miller have found no significant differences in immunoglobulin levels and complement activity between irradiated and control monkeys. A considerable variation in levels of IgG and IgA were found in both the aged controls and irradiated monkeys. The investigators also noted that the frequency of autoantibodies, e.g., anti-reticulin, was higher in the control monkey than in the irradiated animals. The number of monkeys studied for changes in cellular immunity has been small, but there is a suggestion that the T cell responses are less in the irradiated animals compared to the controls. It is important that this finding be fully investigated. Others have claimed that prolonged spaceflight may result in depressed immune function. The cause of the decreased function is thought to be reduced gravity, but the evidence is weak and the mechanism unknown. It will be important to allay concerns about a potential reduction in immunocompetence whether the potential cause is microgravity, radiation, or an interaction between the two.

It was the impression of the panel that the immunological studies were not fully integrated into the overall study. For example, there was no mention of the possibilities of correlating the immunological findings with the clinical and pathological findings. The correlation of changes in immunoglobulins and the presence of amyloid and other degenerative changes should be examined. The studies on the monkeys could give important information about aging and the late effects of high total doses of protons on the immune system. Such studies should be carried out with vigor.

If the full potential of the monkey colony as a resource for information about aging and proton radiation on the immune system is to be exploited, some new protocols must be considered. More detailed evaluation of cellular immunity should include evaluations of B and T cells, subsets of T cells, the humoral response, and response to various mitogens on a larger number of animals than has been carried out so far. Perhaps some animals can be dedicated to these studies.

Diabetes

Diabetes is another example of how the monkeys in the colony can provide a model for study relevant to human disease. The colony provides a great opportunity for an in-depth study of diabetes in a nonhuman primate model that can help in understanding the human disease. The resource is so valuable and has such potential for producing important information that funding for additional studies should be sought. The opportunity for collaborative studies with Dr. Charles F. Howard of the Oregon Regional Primate Research Center should be explored.

Anatomic Pathology

One of the problems of a research project that lasts for decades and involves a number of changes in staffing is the maintenance of quality and consistency. There has been remarkable continuity of the histopathological studies, but, although they have become more detailed and systematic in the last decade, they are not well integrated with the other aspects of the study. The description of the pathological findings is heavily weighted toward the anatomical and histological description of tumors. There was much less information presented about the pathological and aging changes than about neoplasms. Here again, negative findings are of great importance. What should eventually come from these studies is an overall assessment of the neoplastic and nonneoplastic changes with age and in relation to radiation exposure. Further information should be obtained on the correlation between hot spots and the origin of the CNS tumors.

Exposure to low energy protons occurs in space, and in the case of solar particle events, astronauts in deep space could receive considerable doses to the skin. Both the pathology and site of tumors of the skin and the radiation-induced changes in the dermis are of particular interest and relevance to NASA. It was not clear how many of the denoted skin neoplasms were dermal or subcutaneous in origin. The correlation of proton energy and dose with the skin lesions should be investigated.

The panel stressed the importance of the histopathological studies, and it is hoped that more can be accomplished in the investigation of both the time- and dose-dependent changes in tissues. From the examination of the tissues of monkeys that died at different ages, it may be possible to investigate some of the pathogenesis of the disease processes involved.

SUMMARY AND RECOMMENDATIONS

The panel was unanimous in their support for the continuation and extension of the studies on this remarkable colony of monkeys. The value of the colony as a resource for studies, not only of the effects of proton radiation, but of aging, is very great. The colony should be maintained as long as useful information can be obtained. It is impossible to predict precisely how long that will be and the panel suggests that the situation should be reassessed in 5 years.

The colony has been maintained with great dedication and success; in fact, with such success that the colony is now a unique resource. The aim of determining the effects of proton irradiation has governed, to a large extent, the type of longitudinal studies carried out and therefore some of the studies that the committee considered important have not been undertaken. Now is the time to take stock and assess what information can be obtained from the remaining animals and stored material. A close examination of the number of animals in the control and various radiation dose groups should be made and it should be decided how the remaining animals can be used to the greatest advantage. It is suggested that consultation with experts in each of the particular research fields should be considered in order to make the best choices for possible future studies. The panel has made a number of recommendations about areas of investigations that should be pursued or expanded.

A major concern of the panel is that the research program has been too isolated. The program could have benefited from postdoctoral appointees and graduate students doing their thesis work. Perhaps it is not too late to consider such a plan. The panel felt that there were a number of areas of research that might have been considered by the USAF group but were not discussed and which might be included in the future. For example, the brains have been examined for tumors, but much more might be learned about the effects of aging and radiation on the nervous system if the modern techniques used in neuroscience were applied. Behavior is another area that should be considered, in particular, behavior associated with motor function such as balance, muscle coordination, etc. Yet another area are the changes with age in bone and muscle, especially in the females irradiated as juveniles.

There are now many techniques in molecular biology that could be applied to the tissues of the monkeys, and experts that might become collaborators should be contacted. We would reiterate the importance of storing cells and tissues for such studies.

A number of investigators at other institutions have been suggested as possible collaborators or consultants for specific aspects of the program, and a list is appended of researchers in the various pertinent disciplines that might be considered. In both the mortality and cancer studies, and in fact for many of the other studies, the committee thought that more biostatistical analysis could help a great deal in the interpretation of the data.

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APPENDIX A

LIST OF PANEL MEMBERS

R. J. M. Fry, M.D. (Chairman)
Oak Ridge National Laboratory
Biology Division
P.O. Box 2009
Bear Creek Road
Oak Ridge, TN 37831-8077

James A. Joseph, Ph.D.
Gerontology Research Center
National Institute of Aging
Frances Scott Key Medical Center
Baltimore, MD 21224

George W. Casarett, Ph.D.
Department of Biophysics
University of Rochester Medical Center
601 Elmwood Avenue
Rochester, NY 14642

Harold M. McClure, D.V.M.
Associate Director
Yerkes Regional Primate Research Center
Emory University
Atlanta, GA 30322

Douglas Grahn, Ph.D.
Retired
Division of Biological & Medical Research
Argonne National Laboratory
9700 South Cass Avenue
Argonne, IL 60439

Warren K. Sinclair, Ph.D.
President
National Council for Radiation Protection & Measurements
7910 Woodmont Avenue, Suite 1016
Bethesda, MD 20814

Philip Archer, Sc.D.
Professor & Acting Chairman
Dept. of Preventive Medicine
Univ. of Colorado School of Medicine
Box B119, 4200 E. 9th Avenue
Denver, CO 80262

Percival D. McCormack, M.D., Ph.D.
Life Science Division, Code EBM
NASA Headquarters
Room 300, Federal Bldg. 10
Washington, D.C. 20546

Matt J. Kessler, D.V.M.
Director
Caribbean Primate Research Center
P.O. Box 1053
Sabana Seca, Puerto Rico 00749

APPENDIX B

PRESENTATIONS AT THE CONFERENCE ON 9-10 MARCH 1989

1. OVERVIEW
   D. Wood, D.V.M., Ph.D., USAFSAM

2. EXPOSURE DATA & DOSE DISTRIBUTIONS
   K. Hardy, M.S., USAFSAM

3. MORTALITY EXPERIENCE
   D. Wood, D.V.M., Ph.D., USAFSAM

4. CATARACTOGENESIS
   A. C. Lee, D.V.M., J. T. Lett, Ph.D., Colorado State University

5. CANCER RISK
   D. Wood, D.V.M., Ph.D., USAFSAM

6. ENDOMETRIOSIS
   J. Fanton, D.V.M., M.S., J. Golden, D.V.M., USAFSAM

7. HEMATOLOGY & BIOCHEMISTRY
   Y. Salmon, M.A., P. Crump, Ph.D., USAFSAM

8. DIABETES
   D. Wood, D.V.M., Ph.D., USAFSAM

9. INDUCED RADIOSENSITIVITY
   J. Wigle, Ph.D., USAFSAM

10. IMMUNOCOMPETENCE
    W. Stone, Ph.D., Trinity University, M. Miller, M.D., University of Texas Health Science Center at San Antonio

11. SKIN EFFECTS
    A. B. Cox, Ph.D., USAFSAM

12. ANATOMIC PATHOLOGY
    H. Davis, D.V.M., M.S., USAFSAM, G. Hubbard, D.V.M., M.S., Southwest Foundation for Biomedical Research

APPENDIX C

LIST OF EXPERTS IN RESEARCH AREAS RELATED
TO THE LONG-TERM RHESUS MONKEY STUDY

Name	Address	Research Area
Dr. W.P. Dmowski	Rush Presbyterian St. Luke's Medical Center 600 S. Paulina Street Chicago, IL 60612	Endometriosis
Dr. D.M. Bowden	Regional Primate Research Center SJ-50 University of Washington Seattle, WA 98195	Primate Gerontology
Dr. K.R. Brizzee	Delta Regional Primate Research Center Covington, LA 70433	Primate Gerontology
Dr. M. Ordy	Pennwalt Pharmaceuticals Rochester, NY 14623	Primate Gerontology
Dr. E.J. Masoro	Department of Physiology University of Texas Health Science Center San Antonio, TX 78284	Primate Gerontology
Dr. M. Katz	Audie L. Murphy Veterans Memorial Hospital 7400 Morton Minter Dr San Antonio, TX 78284	Gerontology and Endocrinology
Dr. A. Harris	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Behavior
Dr. M. Landauer	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Behavior
Dr. P. Mele	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Behavior
Dr. K. Ingram	Gerontology Research Center National Institute of Aging (NIA) Francis Scott Key Medical Center Baltimore, MD 21224	Behavior

Name	Address	Research Area
Dr. J.A. Joseph	Gerontology Research Center National Institute of Aging (NIA) Francis Scott Key Medical Center Baltimore, MD 21224	Behavior and neuroscience
Dr. R. Wilcox	University of Texas Austin, TX 78767	Behavior and neuroscience
Dr. A. Mickley	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Neuroscience
Dr. W. Hunt	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Neuroscience
Dr. W. Blakely	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Molecular Biology
Dr. T. Walden	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Molecular Biology
Dr. D. McClain	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Molecular Biology
Dr. N. Holbrook	Gerontology Research Center National Institute of Aging (NIA) Francis Scott Key Medical Center Baltimore, MD 21224	Gerontology
Dr. T. MacVittie	Armed Forces Radiobiology Research Institute Bethesda, MD 20814-5415	Hematology and Immunology
Dr. M.B. Kay	Olin E. Teague Veterans Center 1901 South First St Temple, TX 76504	Immunology
Dr. G. Littlefield	Medical Division, Oak Ridge Associated Universities (ORAU) Oak Ridge, TN 37830	Cytogenetics
Dr. J. Preston	Biology Division Oak Ridge National Laboratory (ORNL) Oak Ridge, TN 37831	Radiobiology

Name	Address	Research Area
Dr. A.L. Brooks	Inhalation Toxicology Research Institute Lovelace Foundation, P.O. Box 5890 Albuquerque, NM 87115	Radiobiology
Dr. C.E. Land and Dr. S. Jablon	Radiation Epidemiology Branch National Cancer Institute Bethesda, MD 20814	Statistics
Dr. E. Frome	Engineering Physics and Mathematics Oak Ridge National Laboratory Oak Ridge, TN 37831	Statistics
Dr. E. Lakatta	Gerontology Research Center National Institute of Aging (NIA) Francis Scott Key Medical Center Baltimore, MD 21224	Cardiovascular
Dr. H. Suit	Department of Radiation Medicine Massachusetts General Hospital Boston, MA 02114	Proton Effects
Dr. M. Goitein	Department of Radiation Medicine Massachusetts General Hospital Boston, MA 02114	Proton Dosimetry
Dr. J. Hopewell	University of Oxford Oxfordshire Health Authority Research Institute The Churchill Hospital Headington, Oxford OX3 7LJ, England	Radiation Effects on Skin
Dr. C. Potten	Department of Epithelial Kinetics Paterson Laboratory Christie Hospital & Holt Radium Institute Manchester M20 9BX, England	Radiation Effects on Skin
Dr. C.F. Howard, Jr.	Oregon Regional Primate Research Center 505 N.W. 185th Avenue Beaverton, OR 97006	Diabetes
Dr. E.A. Blakely	Lawrence Berkeley Laboratory University of California Building 10-209 Berkeley, CA 94720	Radiobiology

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